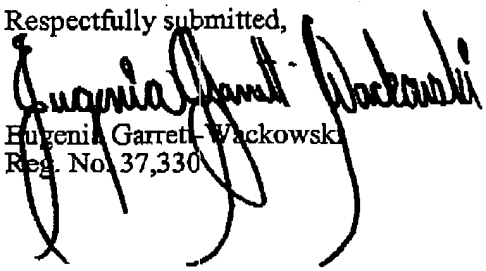
and Eugenia Garrett-Wackowski on April 15, 2003, claims 12 and 16 have been amended. Applicants thanks Examiner Schnizer for his time and attention to matter.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000. x 3005

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

7 ~~12.~~ (Thrice Amended) The combination of:

(i) a DNA construct for integration into the genome of an eukaryotic cell comprising a sequence encoding a first indicator component under the control of a promoter having restricted expression; and

(ii) a DNA construct for integration into the genome of a eukaryotic cell, comprising in the 5' to 3' direction, a splice acceptor, a sequence encoding a second indicator component not operably linked to a transcription control element, and an optional IRES, wherein expression of both the first and second indicator components in said cell is detectable, and wherein [in the absence o either indicator component, there is no detectable indicator] if said first indicator component is an antibiotic resistance marker, said second indicator component is not an antibiotic resistance marker.

16. (Amended) [The] A method of [claim 1] screening for the integration of a DNA construct into a target gene having restricted expression in a mouse, said method comprising:

(i) transforming a mouse ES cell with a first DNA construct encoding a first indicator component linked to a promoter having restricted expression in a mouse, wherein DNA encoding the first indicator component is separated from said promoter by a sequence of DNA which prevents transcriptional control by said promoter over the DNA encoding the first indicator component;

(ii) transforming the cell of (i) or a descendent of the cell by operably integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells of (ii); and

(iv) monitoring the tissue or specialized cells of (iii) for a detectable indicator resulting from both the first and second indicator components indicative of

integration of the second DNA construct into a gene having restricted expression,
wherein[:

(i) in the first DNA construct, DNA encoding the first indicator component is separated from the promoter having restricted expression by a sequence of DNA which prevents transcriptional control by said promoter over the DNA encoding the first indicator component;

(ii)] in the second DNA construct, the second indicator component is a recombinase capable of removing the sequence of DNA preventing transcriptional control in the first DNA construct; and,

wherein said monitoring is for cells in which the first indicator component is expressed under the transcriptional control of the promoter having restricted expression.